

L123 ANSWER 6 OF 8 WPIX (C) 2003 THOMSON DERWENT

AN 1999-005164 [01] WPIX

DNC C1999-001647

TI Agent for increasing bone density - contains oestrogen and aromatase non-metabolisable androgen.

DC B01

PA (KAKE) KAKEN PHARM CO LTD

CYC 1

PI JP 10279483 A 19981020 (199901)* 10p A61K031-565

ADT JP 10279483 A JP 1998-22353 19980203

PRAI JP 1997-21451 19970204

IC ICM A61K031-565

AB JP 10279483 A UPAB: 19990107

Agent for treating osteoporosis or retarded osteogenesis contains oestrogen preferably oestradiol and aromatase non-metabolisable androgen preferably dihydrotestosterone. Also claimed are a kit containing oestrogen and aromatase non metabolisable androgen in a composition comprising the kit, a method preferably by oral, percutaneous, implant or subcutaneous application for increasing bone density includes administering oestrogen having activity corresponding to 0.2-2 (preferably 0.2-1) $\mu\text{g/kg/day}$ oestradiol, simultaneously or separately with aromatase non metabolisable androgen having activity preferably corresponding to 20-80 $\mu\text{g/kg/day}$ dihydrotestosterone, a machine readable memory media which records a program for carrying out the methods and an administration system for administration of estrogen and aromatase non metabolisable androgen.

The estrogen is preferably oestradiol, oestradiol valerate, oestradiol benzoate, oestradiol propionate, oestrone, estrogen conjugate or estriol propionate and the aromatase non metabolisable androgen is dihydrotestosterone, oxandrolone, oxymetholone, stanozolol, mestanolone, stanolone or androstane.

USE - The composition is used for treating osteoporosis or retarded osteogenesis.

ADVANTAGE - The composition maintains or increases bone density without side effects.

Dwg.0/3

FS CPI

FA AB; DCN

MC CPI: B01-A02; B01-C05; B14-N01

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L8 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
 AN 1992:564103 CAPLUS
 DN 117:164103
 TI **Progestin** antagonism of estrogen stimulated 1,25-dihydroxyvitamin D levels
 AU Bikle, Daniel D.; Halloran, Bernard P.; Harris, Steven T.; Portale, Anthony A.
 CS VA Med. Cent., UCSF Med. Serv., San Francisco, CA, 94121, USA
 SO Journal of Clinical Endocrinology and Metabolism (1992), 75(2), 519-23
 CODEN: JCEMAZ; ISSN: 0021-972X
 DT Journal
 LA English
 CC 2-4 (Mammalian Hormones)
 AB Progestins are frequently used in combination with estrogen to prevent or treat postmenopausal **osteoporosis**. Progestins protect against the undesirable hyperplastic effects of estrogen on the endometrium. The possibility that progestins might antagonize the beneficial effects of estrogen on calcium homeostasis has received little attention. In this study the authors detd. whether the addn. of **progestin** to estrogen would alter the ability of estrogen to raise serum 1,25-dihydroxyvitamin D [1,25-(OH)2D] levels. Women within 5 yr of menopause were treated with three cycles of oral unopposed estrogen [1 or 2 mg/day (3.67 or 7.34 .mu.mol/day) 17.beta.-estradiol (E2) for 25/30 days of each cycle] followed by three cycles of E2 plus **progestin** [10 mg/day (29 .mu.mol/day) medroxyprogesterone on days 12-25]. E2 increased both total and free 1,25-(OH)2D concns. in a dose-dependent fashion. These levels increased progressively over the three cycles of unopposed estrogen treatment. In contrast the vitamin D binding protein concn. reached maximal levels after one cycle of E2. With the addn. of **progestin**, the levels of total and free 1,25-(OH)2D returned toward baseline although vitamin D binding protein levels remained elevated. PTH levels rose with both doses of E2 as serum calcium levels fell. **Progestin** did not significantly alter the effects of E2 on PTH or calcium. These results raise the possibility that **progestin** may antagonize part of the salubrious effects of estrogen on calcium homeostasis.
 ST calcitriol estradiol progestin calcium serum
 IT Progestogens
 RL: BIOL (Biological study)
 (calcitriol of blood serum response to estradiol modulation by, in women)
 IT Blood serum
 (calcitriol of, of women, estradiol and progestin effect on)
 IT Proteins, specific or class
 RL: BIOL (Biological study)
 (dihydroxyvitamin D3-binding, of blood serum, of women, estradiol and progestin effect on)
 IT 520-85-4, Medroxyprogesterone
 RL: BIOL (Biological study)
 (calcitriol of blood serum response to estradiol modulation by, in women)
 IT 50-28-2, Estradiol, biological studies
 RL: BIOL (Biological study)
 (calcitriol of blood serum response to, in women, progestin effect on)
 IT 7440-70-2, Calcium, biological studies 9002-64-6, Parathormone
 32222-06-3, Calcitriol
 RL: BIOL (Biological study)
 (of blood serum, of women, estradiol and progestin effect on)

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